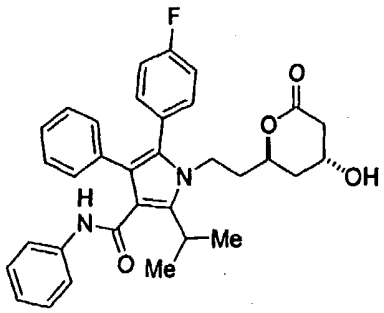
CLAIMS

What is claimed is:

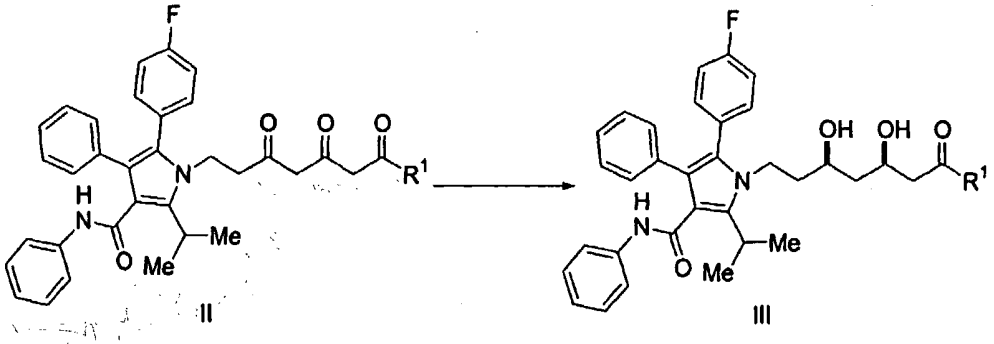
1. A process for the preparation of a compound of formula (I)



I

comprising:

(a) contacting in a solvent a compound of formula (II) with a transition metal catalyst, a hydrogen source, and a base wherein the base is selected from the group consisting of NaOH and an amine base, to give a compound of formula (III):



II III

wherein

R^1 is defined as –XR, wherein X is O,

S, or Se, or

R^1 is $\begin{matrix} N{-\!-}R^2 \\ | \\ R^3 \end{matrix}$, wherein R^2 and R^3 are independently alkyl,

cycloalkyl,

arylalkyl, or

aryl, or

R^2 and R^3 taken together are $-(CH_2)_4-$,

$-(CH_2)_5-$,

$-(CH(R^4)-CH_2)_3-$,

$-(CH(R^4)-CH_2)_4-$,

$-(CH(R^4)-(CH_2)_2-CH(R^4))-$,

$-(CH(R^4)-(CH_2)_3-CH(R^4))-$,

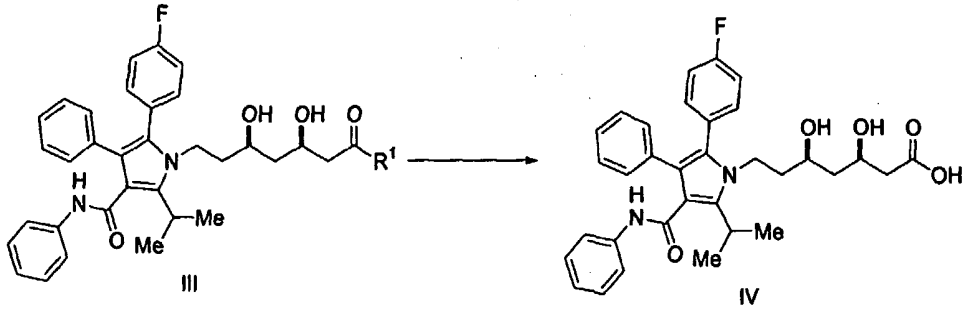
$-CH_2-CH_2-A-CH_2-CH_2-$,

$-CH(R^4)-CH_2-A-CH_2CH_2-$,

$-CH(R^4)-CH_2-A-CH_2-CH(R^4)-$,

wherein R^4 is alkyl of from one to four carbon atoms, A is O, S, or N and R is defined as alkyl, aryl, arylalkyl, or heteroaryl;

(b) conversion of the compound of formula (III) wherein R^1 is as defined above to a compound of formula (IV) using base in aqueous methanol or aqueous THF;



and

(c) contacting in a solvent the compound of formula (IV) with an acid to afford a compound of Formula (I).

2. The process of claim 1, wherein contacting in step (a) comprises mixing the compound of formula I, formic acid, base, and transition metal catalyst in a solvent to form a homogeneous or heterogeneous mixture.

3. The process of claim 2, wherein the solvent in step (a) is an aqueous or anhydrous polar aprotic polar protic, or nonpolar solvent, a ketone, pentane, or hexane, or mixtures thereof.

4. The process of claim 2, wherein the solvent in step (a) is selected from tetrahydrofuran, dimethyl formamide, diethyl ether, methylene chloride, chloroform, methanol, ethanol, isopropanol, and toluene, acetonitrile, ethyl acetate, water, or mixtures or combinations thereof.

5. The process of claim 1, wherein in the compound of formula II or III, R^1 is defined as –XR, wherein X is O and R is alkyl,
cycloalkyl,
arylalkyl,
aryl, or
heteroaryl.

6. The process of claim 1, wherein in the compound of formula II or III, R^1 is defined as –XR, wherein X is O and R is alkyl.

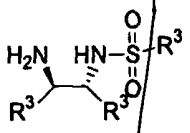
7. The process of claim 1, wherein in the compound of formula II or III, R^1 is OMe, OEt, or Ot-Bu.

8. The process of claim 1, wherein the transition metal catalyst in step (a) is derived from Ir, Ru, or Rh.

9. The transition metal catalyst of claim 1, wherein the transition metal catalyst is prepared from a transiton metal catalyst precursor and a chiral, non racemic ligand which is a chiral diamine ligand or a chiral alcohol amine ligand.

10. The transition metal catalyst of claim 9, wherein the transition metal catalyst precursor is selected from [dichloro-(1,5-cycloocta-diene)] ruthenium (II) oligomer, $[RuCl_2benzene]_2$, $[RuCl_2p$-cymene$]_2$, $[RuCl_2$ mesitylene$]_2$, [dibromo-(1,5-cyclooctadiene)] ruthenium (II) dimer, [bis-(2-methallyl)cycloocta-1,5-diene] ruthenium (II) complex, pentamethylcyclopenta- dienyl iridium (III)chloride dimer, and pentamethylcyclopentadienyl rhodium (III)chloride dimer.

11. The transition metal catalyst of claim 9, wherein the non racemic ligand is a chiral diamine ligand or a chiral alcohol amine ligand selected from norephedrine or compounds **7** or **8**.



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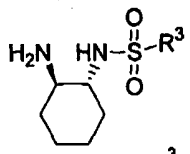


8

R^3=Alkyl, heteroaryl, or aryl

12. The process of claim 1, wherein the hydrogen source in step (a) is formic acid, ammonium formate, or isopropanol.

13. The process of claim 1, wherein the hydrogen source in step (a) is formic acid or ammonium formate.

14. The process of claim 1, wherein the hydrogen source in step (a) is formic acid.

15. The process of claim 1, wherein the base in step (a) is an amine base selected from triethylamine, trimethylamine, ethyldimethylamine, tri-n-propylamine, diisopropylethylamine, 1,8-diazabicyclo[5.4.0.] undec-7-ene (DBU), lutidine, collidine, 4-

dimethylaminomethyl pyridine, diisopropyl amine, tri-n-butyl amine,4-methylmorpholine, piperidine, and pyrrolidine.

16. The process of claim 1, wherein the concentration of the compound of formula (II) in the solvent in step (a) is about 0.2 Molar to about 0.6 Molar.

17. The process of claim 1, wherein the concentration of the compound of formula (II) in the solvent in step (a) is about 0.3 Molar to about 0.5 Molar.

18. The process of claim 1, wherein the concentration of the compound of formula (II) in the solvent in step (a) in the solvent is about 0.35 Molar to about 0.45 Molar.

19. The process of claim 1, wherein in step (a), the molar equivalents of each of the compound of formula (II) used is about 1; of the hydrogen source, the base, and the transition metal catalyst are:

about 1 equivalent of the compound of formula (II);
about 2.0 to about 2.5 equivalents of hydrogen source;
about 4.0 to about 5.0 equivalents of amine base; and
about 0.05 to about 2 mol percent of the transition metal catalyst.

20. The process of claim 1, wherein in step (a), the molar equivalents of each of the compound of formula (II) used is about 1; of the hydrogen source, the base, and the transition metal catalyst are:

about 1 equivalent of the compound of formula (II);
about 2.1 to about 2.4 equivalents of hydrogen source;
about 4.1 to about 4.8 equivalents of amine base; and
about 1 mol percent of the transition metal catalyst.

21. The process of claim 1, wherein the reaction temperature in step (a) is about 0 to about 50 °C.

22. The process of claim 1, wherein the reaction temperature in step (a) is about 10 to about 40 °C.

23. The process of claim 1, wherein the reaction temperature in step (a) is about 20 to about 30 °C.

24. The process of claim 1, wherein the reaction pressure of step (a) is about 0.9 to about 1.1 atmospheres.

25. The process of claim 1, wherein the reaction pressure of step (a) is about 0.95 to about 1.05 atmospheres.

26. The process of claim 1, wherein the reaction pressure of step (a) is about 0.99 to about 1.02 atmospheres.

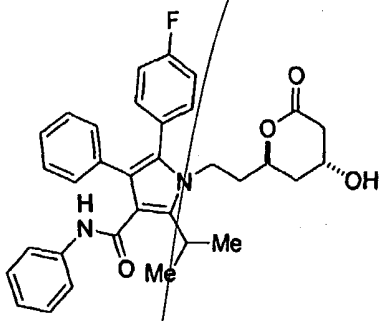
27. The process of claim 1, wherein the reaction time of step (a) is about 6 to about 24 hours.

28. The process of claim 1, wherein the reaction time of step (a) is about 12 to about 18 hours.

29. The process of claim 1 wherein the base used in step (b) is KOH.

30. The process of claim 1 wherein the acid used in step (c) is aqueous HCl.

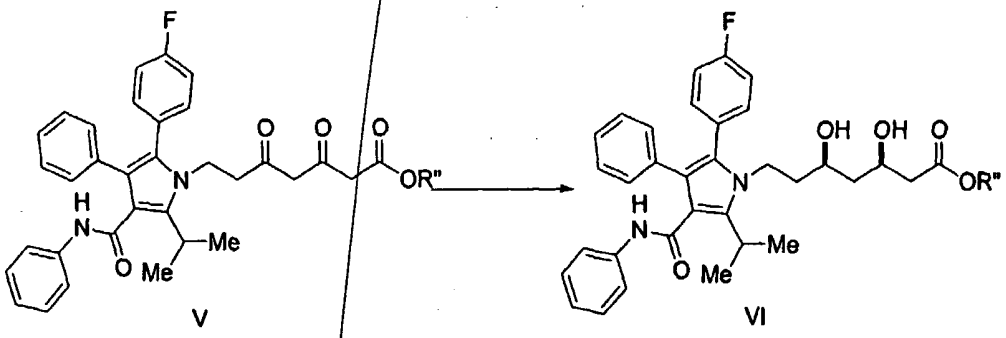
31. A process for the preparation of a compound of formula (I)



I

comprising:

(a) contacting a compound of formula (V) with a transition metal catalyst, a hydrogen source, and a base to give a compound of formula (VI):

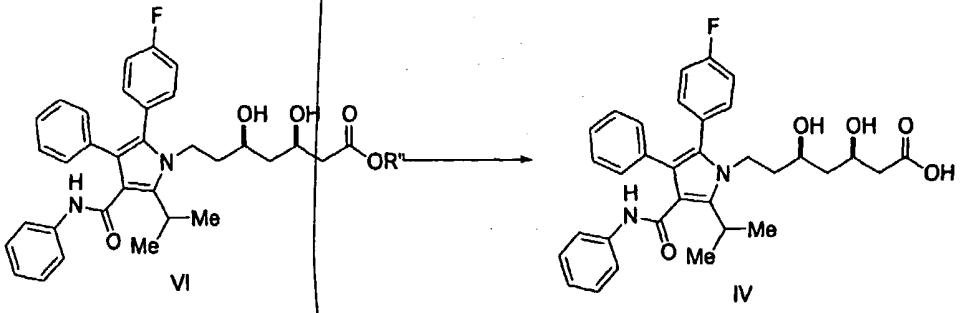


V VI

wherein

R" is defined as Me, Et, or t-Bu;

(b) conversion of the compound of formula (VI) wherein R" is as defined above to a compound of formula (IV);



VI IV

and

(c) contacting in a solvent the compound of formula (IV) with an acid to afford a compound of Formula (I).

32. The process of claim 31, wherein contacting in step (a) comprises mixing the compound of formula V, formic acid, base, and transition metal catalyst in a solvent to form a homogeneous or heterogeneous mixture.

33. The process of claim 32, wherein the solvent in step (a) is an aqueous or anhydrous polar aprotic/polar protic, or nonpolar solvent, a ketone, or hexane.

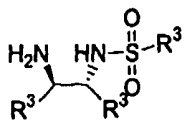
34. The process of claim 32, wherein the solvent in step (a) is selected from tetrahydrofuran, dimethyl formamide, diethyl ether, methylene chloride, chloroform, methanol, ethanol, isopropanol, and toluene, acetonitrile, ethyl acetate, water, or mixtures or combinations thereof.

35. The process of claim 31, wherein the transition metal catalyst in step (a) is derived from Ir, Ru, or Rh.

36 The transition metal catalyst of claim 35, wherein the transition metal catalyst is prepared from a transition metal catalyst precursor and a chiral, non racemic ligand.

37. The transition metal catalyst of claim 35 wherein the transition metal catalyst precursor is selected from [dichloro-(1,5-cycloocta-diene)] ruthenium (II) oligomer, $[RuCl_2benzene]_2$, $[RuCl_2p\text{-}cymene]_2$, $[RuCl_2$ mesitylene$]_2$, [dibromo-(1,5-cyclooctadiene)] ruthenium (II) dimer, [bis-(2-methallyl)cycloocta-1,5-diene] ruthenium (II) complex, pentamethylcyclopenta- dienyl iridium (III)chloride dimer, and pentamethylcyclopentadienyl rhodium (III)chloride dimer.

38. The transition metal catalyst of claim 35 wherein the non racemic ligand is a chiral diamine ligand or a chiral alcohol amine ligand selected from norephedrine or compounds 7 or 8.



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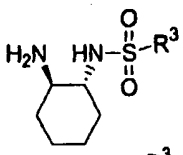

8

R^3=Alkyl, heteroaryl, or aryl

39. The process of claim 31, wherein the hydrogen source in step (a) is formic acid, ammonium formate, or isopropanol.

40. The process of claim 31, wherein the hydrogen source in step (a) is formic acid or ammonium formate

41. The process of claim 31, wherein the hydrogen source in step (a) is formic acid.

42. The process of claim 31, wherein the base in step (a) is an amine base selected from triethylamine, trimethylamine, ethyldimethylamine, tri-n-propylamine, diisopropylethylamine, 1,8-diazabicyclo[5.4.0.] undec-7-ene (DBU), lutidine, collidine, 4-dimethylaminomethyl pyridine, diisopropyl amine, tri-n-butyl amine, 4-methylmorpholine, piperidine, and pyrrolidine.

43. The process of claim 31, wherein the concentration of the compound of formula (V) in the solvent in step (a) is about 0.2 Molar to about 0.6 Molar.

44. The process of claim 31, wherein the concentration of the compound of formula (V) in the solvent in step (a) is about 0.3 Molar to about 0.5 Molar.

45. The process of claim 31, wherein the concentration of the compound of formula (V) in the solvent in step (a) in the solvent is about 0.35 Molar to about 0.45 Molar.

46. The process of claim 31, wherein in step (a), the molar equivalents of each of the compound of formula (V) used is about 1; of the hydrogen source, the base, and the transition metal catalyst are:

about 1 equivalent of the compound of formula (V);
about 2.0 to about 2.5 equivalents of hydrogen source;
about 4.0 to about 5.0 equivalents of amine base; and
about 0.05 to about 2 mol percent of the transition metal catalyst.

47. The process of claim 31, wherein in step (a), the molar equivalents of each of the compound of formula (V) used is about 1; of the hydrogen source, the base, and the transition metal catalyst are:

about 1 equivalent of the compound of formula (V);
about 2.1 to about 2.4 equivalents of hydrogen source;
about 4.1 to about 4.8 equivalents of amine base; and
about 1 mol percent of the transition metal catalyst.

48. The process of claim 31, wherein the reaction temperature of step (a) is about 0 to about 50 °C.

49. The process of claim 31, wherein the reaction temperature of step (a) is about 10 to about 40 °C.

50. The process of claim 31, wherein the reaction temperature of step (a) is about 20 to about 30 °C.

51. The process of claim 31, wherein the reaction pressure of step (a) is about 0.9 to about 1.1 atmospheres.

54. The process of claim 31, wherein the reaction pressure of step (a) is about 0.95 to about 1.05 atmospheres.

55. The process of claim 31, wherein the reaction pressure of step (a) is about 0.99 to about 1.02 atmospheres.

56. The process of claim 31, wherein the reaction time of step (a) is about 6 to about 24 hours.

57. The process of claim 31, wherein the reaction time of step (a) is about 12 to about 18 hours.

58. The process of claim 31 wherein the base used in step (b) is KOH.

59. The process of claim 31 wherein the acid used in step (c) is aqueous HCl.